

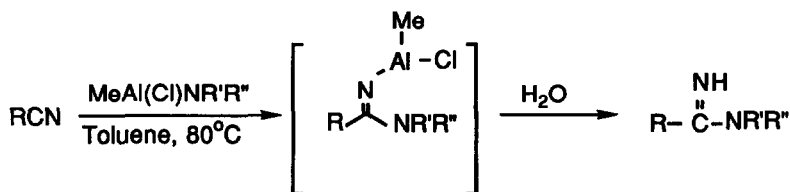
## AN EFFICIENT CONVERSION OF NITRILES TO AMIDINES

Ravi S. Garigipati

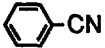
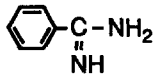
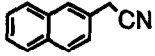
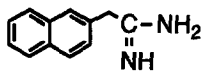
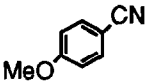
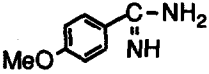
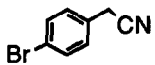
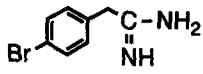
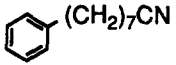
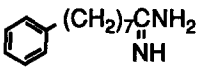
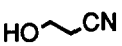
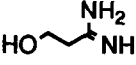
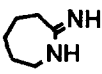
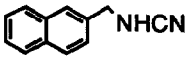
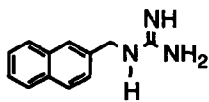
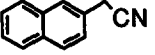
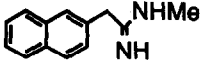
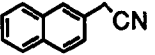
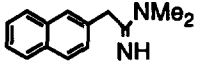
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**Abstract:** A convenient method has been developed for direct conversion of nitriles to amidines in high yields. The method can also be applied to the preparation of guanidines from N-alkyl cyanamides.

An efficient one step preparation of an amidine by the direct nucleophilic addition of an amine to the parent nitrile is an extremely desirable transformation for which no mild and practical methods exist.<sup>1</sup> Methods currently available for amidine synthesis involve multistep processes which proceed in moderate to poor yields.<sup>1</sup> Weinreb *et al.* have demonstrated that aluminum amides efficiently add to carboxylic esters to afford the corresponding carboxamides in a single step.<sup>2</sup> We reasoned that these aluminum amides might similarly add to nitriles, thus affording amidines. Insertion of diethylaluminum dimethylamide into benzonitrile was first studied in 1969.<sup>4</sup> In these early studies<sup>3,4</sup> dimeric aluminum amidine derivatives were isolated and studied spectroscopically. However, the application of these reagents for the preparation of amidines was never demonstrated. Apart from these preliminary studies, there are no reports of the use of aluminum amides in the preparative conversion of nitriles to amidines.<sup>5</sup> We have found that alkylchloroaluminum amides, which are conveniently generated from trimethyl aluminum and ammonium chloride or amine hydrochlorides,<sup>2b</sup> efficiently add to nitriles and afford the desired amidines in high yields.



**Table.** Preparation of Amidines from Nitriles

Entry	Nitrile	Aluminum Amide	Amidine <sup>10</sup>	Yield (%) <sup>b</sup>
1.		MeAl(Cl)NH <sub>2</sub>		80
2.		MeAl(Cl)NH <sub>2</sub>		95
3.		MeAl(Cl)NH <sub>2</sub>		96
4.		MeAl(Cl)NH <sub>2</sub>		88
5.		MeAl(Cl)NH <sub>2</sub>		93
6.		MeAl(Cl)NH <sub>2</sub>		78 <sup>a</sup>
7.	HCl.H <sub>2</sub> N(CH <sub>2</sub> ) <sub>6</sub> CN	—		88
8.		MeAl(Cl)NH <sub>2</sub>		77
9.		MeAl(Cl)NHMe		94
10.		MeAl(Cl)NMe <sub>2</sub>		60

a. A 15% yield of acrylamidine was also obtained.

b. Isolated yields.

The addition of methyl chloroaluminum amides to nitriles is quite general (Table). Alkyl, benzyl and aryl amidines may be prepared in high yield from the

corresponding nitriles, while mono- and disubstituted amidines are obtained from the addition of the appropriately N- substituted methyl chloroaluminum amides. Both inter and intramolecular additions may be carried out. 6-Aminocapronitrile hydrochloride can be converted to the corresponding aluminum amide by treatment with trimethylaluminum, which undergoes cyclization *in situ* to afford caprolactamidine in high yield (entry 7).

We also examined the applicability of this methodology to the preparation of guanidines. N-(2-Naphthylmethyl)cyanamide<sup>7</sup> can be transformed to the corresponding guanidine under similar reaction conditions. It should be noted that dialkylaluminum amides are sluggish in reacting with nitriles as compared to the chloroalkylaluminum amides. For instance the dimethyl aluminum amide derived from 6-aminocapronitrile is resistant to cyclization whereas the corresponding methyl chloroaluminum amide yields caprolactamidine in a good yield (*vide supra*).

In a typical experiment a solution of the nitrile (3.0 mmol) in 2.0 mL of dry toluene was added to a 1.25 M solution of the aluminum amide reagent<sup>9</sup> in toluene at room temperature. This solution was heated under argon at 80 °C until the nitrile was consumed (6-20 hrs, as followed by TLC). The reaction mixture was cooled and the aluminum complex was decomposed by carefully pouring the solution into a slurry of silica gel (20g) in chloroform. The mixture was stirred for 5 min and the silica gel was filtered. The filtercake was further washed with methanol (100 mL). Evaporation of the filtrate and crystallization of the residue yielded the requisite amidine.

Thus, the addition of alkylchloroaluminum amides to nitriles and N-substituted cyanamides provides a general one step procedure to prepare amidines and guanidines under mild conditions.

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5. The only preparative conversion of nitriles to amidines was reported<sup>6</sup> in a stepwise process via N,N,N'-tris(trimethylsilyl) amidines.
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7. N-(2-Naphthylmethyl) cyanamide was prepared by alkylation of 2-naphthylamine with cyanogen bromide.<sup>8</sup>
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9. The methylchloro aluminum amide reagent was prepared according to the standard Weinreb procedure.<sup>2b</sup>
10. All the products were characterized by spectroscopic techniques (IR; NMR; MS) and elemental analysis or HRMS.

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